

Exhibit 1

**UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA**

ALLERGAN USA, INC., and
ALLERGAN INDUSTRIE, SAS,

Plaintiffs,

v.

MEDICIS AESTHETICS, INC.,
MEDICIS PHARMACEUTICAL CORP.,
VALEANT PHARMACEUTICALS NORTH
AMERICA LLC,
VALEANT PHARMACEUTICALS
INTERNATIONAL, VALEANT
PHARMACEUTICALS INTERNATIONAL,
INC., AND GALDERMA LABORATORIES,
L.P.

Defendants.

Case No. SACV13-01436 AG (JPRx)

EXPERT REPORT OF MARY LUPO, M.D.

B. HA Dermal Fillers without Lidocaine

38. There were several HA dermal fillers that did not include lidocaine on the market in the U.S. prior to the introduction of Juvéderm Ultra XC and Juvéderm Ultra Plus XC.

39. Before Juvéderm XC was introduced in the United States, Allergan marketed Juvéderm Ultra and Juvéderm Ultra Plus. These products were HA fillers, but lacked lidocaine. Allergan introduced these products in the United States in 2006, and I first used them in my practice in 2006, as soon as they were FDA-approved and available.

40. Similarly, before Restylane-L and Perlane-L were introduced in the United States, Medicis marketed Restylane and Perlane. These products were HA fillers, and they too lacked lidocaine. Medicis introduced Restylane in the United States in 2003 and Perlane in the United States in 2007. I first used them in my practice as soon as each was FDA-approved and available in the United States.

41. In about 2004, the FDA approved the Hylaform family of dermal fillers. Hylaform was an animal-derived HA filler that ultimately led to spin off products like Captique and Prevelle SILK.²⁸ Hylaform, which did not contain lidocaine, is no longer on the market in the United States.²⁹ Unlike the Juvéderm family of fillers, Hylaform had a very short duration of action—approximately three to four months.³⁰

42. In contrast to collagen, HA dermal fillers have very low allergenicity.³¹ This characteristic of HA fillers relieves patients and injectors of the lengthy waiting period required for collagen products and allows patients to be treated on the same day as their consultation with their injector. Moreover, HA's physical properties make it much better suited for the treatment

²⁸ Baumann at 198.

²⁹ *Id.*

³⁰ Baumann, *Dermal Fillers*, at 198-99.

³¹ Baumann, *Dermal Fillers*, at 196.

of moderate to severe facial wrinkles and folds and more durable than bio-engineered human collagen products. However, HA dermal fillers without lidocaine were associated with significant pain.

C. Managing Pain Associated with Dermal Filler Injections

43. Prior to the introduction of Juvéderm Ultra XC and Juvéderm Ultra Plus XC, pain was a major issue associated with HA fillers. I noted this in my practice, and it was well-documented in the literature.³²

44. In my clinical experience, injecting a dermal filler which does not contain lidocaine is very painful for patients. That pain and discomfort presented several challenges for injectors and patients alike. To overcome these challenges, injectors attempt to mitigate pain in a number of ways, including topical or regional anesthetics and nerve blocks. While I personally prefer topical anesthetics, all anesthetics (local, topical and regional) suffer drawbacks. For instance, they require waiting for the injection sites on the patient to become numb and increase the length of office visits. Several investigators have noted the problems with topical creams and local or regional anesthetics, stating that they can “pose several drawbacks to the routine injection of fillers; for example, they can lengthen and complicate the procedure, and many physicians are unfamiliar with these techniques.”³³ In my experience, longer office visits inconveniences patients, increases cost to patients, and decreases profitability to injectors.

³² See S.H. Weinkle et al., *A multi-center, double-blind, randomized controlled study of the safety and effectiveness of Juvederm injectable gel with and without lidocaine*. J. Cosmetic Dermatol., 2009; 8:205-210, at 205 [AGNHA00180351-56] (“Weinkle”) (“Pain is a common patient complaint during dermal filler injections, and anesthetics are frequently used to make the procedure more comfortable.”); G.D. Monheit et al., *Reduced Pain with Use of Proprietary Hyaluronic Acid with Lidocaine for Correction of Nasolabial Folds: A Patient-Blinded, Prospective, Randomized Controlled Trial*. Dermatol. Surg. 2010; 36:94-101, at 95 [AGNHA00191318-25] (“Monheit”) (“Although several HA products are available, all are associated with notable pain upon injection, and patients consider pain to be a significant factor with injectable implants.”).

³³ P.M. Levy et al., *Comparison of Injection Comfort of a New Category of Cohesive Hyaluronic Acid Filler with Preincorporated Lidocaine and a Hyaluronic Acid Filler Alone*. Dermatol. Surg. 2009; 35:332-37, at 332–33 [AGNHA00180338-43] (“Levy, *Comparison of Injection Comfort*”); see also Weinkle at 205 (“the effects of topic anesthetic are limited and not immediate”); see also Monheit at 95 (“Although effective, these measures add an

in pain due to the lidocaine in the Juvéderm XC products leads to better treatment experiences and outcomes for my patients.

5. Restylane-L and Perlane-L

63. Medcis, Valeant, and now Galderma have marketed the Restylane-L and Perlane-L HA fillers with lidocaine in the U.S. The FDA approved these products January 29, 2010,⁵⁹ and I have used them frequently since their introduction. In clinical trials, patients and injectors found that Restylane-L and Perlane-L relieved pain and increased patient comfort both during and after the procedure in comparison to Restylane and Perlane. For instance, in U.S. study MA-1100-001, “[t]he safety and pain reduction effect of Restylane-L in the treatment of facial folds and wrinkles (nasolabial folds) was evaluated in a prospective randomized controlled clinical study involving 60 patients.” The study found that “[t]he addition of lidocaine to Restylane resulted in a statistically significant reduction in the pain experienced by the patients [and t]he study also showed that the safety profile of Restylane-L was consistent with Restylane.”⁶⁰

V. LONG- FELT NEED

64. As discussed above, prior to the introduction of Juvéderm Ultra XC and Juvéderm Ultra Plus XC, in 2010, there existed a long-felt but unmet need for a HA dermal filler which would have a low risk of allergy, a longer-lasting clinical effect than other available fillers, have acceptable physical characteristics, and provide a relatively pain-free treatment option for patients. That need existed since the shortcomings of the collagen dermal filler products, discussed above, were identified. Moreover, physicians were actively trying to address the need, for example by using local, regional, or topical anesthetics or by “swishing” lidocaine into HA fillers, but, as discussed above, this alternative failed to meet the need at least because it resulted

⁵⁹ Restylane-L and Perlane-L Approval Letter [VAL0057647-52].

⁶⁰ Restylane-L® product information [VAL0085356-57].

in changes to the rheological properties of the gel. Physicians were also encouraging the product manufacturers to introduce an HA filler with anesthetic.

65. Based on my experience, Juvéderm Ultra XC and Juvéderm Ultra Plus XC satisfied that long-felt need, which was felt by patients and injectors alike. Those products offered same-day treatment, marginalized the risk of contamination and allergic reaction, eliminated the cumbersome and contamination-prone process of mixing anesthetics into the dermal filler before injection, and enhanced patient comfort by more effectively eliminating pain associated with treatment. Moreover, incorporating lidocaine into the Juvéderm products achieved all of those things without changing the physical characteristics and performance of the products.

66. In my own practice, many of my patients received dermal filler treatments. When Juvéderm Ultra XC, Juvéderm Ultra Plus XC, Restylane-L, and Perlane-L arrived on the market, I switched every one of my patients who could be safely treated with an HA dermal filler with lidocaine incorporated to one of those products. My patients agreed that Juvéderm Ultra XC, Juvéderm Ultra Plus XC, Restylane-L, and Perlane-L hurt less than products “swished” with lidocaine, and that they provided very quick pain relief. Further, my patients and I noted that treatment with those products lasted longer than treatments with dermal fillers “swished” with lidocaine.

67. As an injector, treating patients with Juvéderm Ultra XC, Juvéderm Ultra Plus XC, Restylane-L, and Perlane-L saved me time and money. To properly “swish” lidocaine into a dermal filler product, injectors must necessarily use a technique to attempt to keep the products sterile, and lower the risk of infection. Proper “swishing” takes time, increasing costs for

patients and injectors alike.⁶¹ Therefore, Juvéderm Ultra XC, Juvéderm Ultra Plus XC, Restylane-L, and Perlane-L, which provided a sterile, premade product including anesthetic and having an acceptable shelf life satisfied a long-felt need for injectors as well.

68. The clinical literature also reflects that Juvéderm Ultra XC and Juvéderm Ultra Plus XC satisfied a well-known market need and supports my own experiences and understanding. For instance, one clinical study reported that “[t]he new category of lidocaine-containing HA fillers addresses a previously unmet patient need for greater injection comfort.”⁶² Another study, which examined patients who received Juvéderm XC in one side of their face and a non-lidocaine dermal filler in the other side, observed that patients and clinicians alike found Juvéderm XC to be as effective as non-lidocaine products and patients found treatment to be more comfortable.⁶³ Similarly, another study found that Juvéderm XC resulted in less patient pain and that the addition of lidocaine did not impact product longevity and treatment duration.⁶⁴

VI. ACCEPTABLE ALTERNATIVES TO THE JUVÉDERM XC PRODUCTS, RESTYLANE-L AND PERLANE-L

69. In my opinion, no other product on the market presents an acceptable alternative to the Juvéderm Ultra XC, Juvéderm Ultra Plus XC, Restylane-L, or Perlane-L. If the Restylane-L and Perlane-L products were not on the market, I would switch those patients to a product in the Juvéderm XC family.

70. I was very impressed with the Juvéderm Ultra XC and Ultra Plus XC products when I first used them following their introduction in January of 2010. I found that there was no

⁶¹ See also Weinkle at 208 (“Not only does this practice [of mixing lidocaine into a dermal filler] prompt questions of sterility, consistency, and quality of the final mixture, but it can also change the product’s flow characteristics and effectiveness by diluting the HA concentration with the lidocaine solution.”).

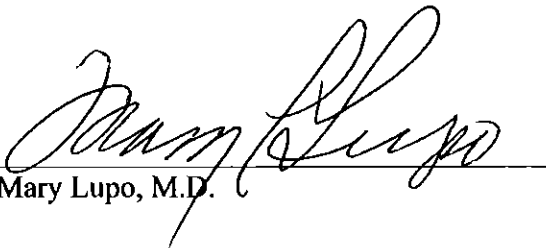
⁶² Levy, *Comparison of Injection Comfort*, at 335.

⁶³ Levy, *A split-face comparison*, at 172.

⁶⁴ H. Raspaldo et al., *Longevity of effects of hyaluronic acid plus lidocaine facial filler*. J Cosmetic Dermatology 2010, 9:11-15, at 13-14 [AGNHA00180164-68].

testimony. Moreover, I may make additions, deletions or modifications in the future that would be reflected in my trial testimony. For trial, I may prepare diagrams, charts and demonstrations that illustrate the issues presented. I also understand that I may be asked to give rebuttal testimony at trial on matters not covered in this expert report.

Dated: February 9, 2015


Mary Lupo, M.D.